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09/435,629	11/08/1999	STEVEN L. STICE	000270-086	5462

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WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/435,629 Examiner Joseph Woitach	STICE ET AL. Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 08 November 1999.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 2-90 is/are pending in the application.
 4a) Of the above claim(s) 2-78 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 79-90 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 08 November 1999 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) The translation of the foreign language provisional application has been received.
 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1632

DETAILED ACTION

This application filed November 8, 1999, is a divisional of 08/766,939, filed December 16, 1996, now US Patent 5,994,619, which is a continuation in part of 08/626,054, filed April 1, 1996, now US Patent 5,905,042.

Election/Restriction

Claims 2-90 are pending. Applicant's election without traverse of group II, claims 79-90, in Paper No. 9 is acknowledged. Claims 2-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Claims 79-90 are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

Please note that the claims to be have inserted as set forth in paper number 3, were not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not

Art Unit: 1632

be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 78-89 have been renumbered 79-90.

Claims 79-90 are objected to for the following informalities: because the claims have been renumbered they no longer recite the correct claim dependency. Claims should be amended to indicate the proper dependency, reflecting claim renumbering. Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities: The Brief Description of the Figures does not comply with 37 CFR 1.74. Specifically, a separate reference to and brief description of each of the drawing(s) must be present in the disclosure.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1632

Claims 82, 83 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 82 is unclear in the recitation of ‘comprising transgenic bovine CICMs’ because of the open language in claim 78 of a ‘stable culture comprising’ it is unclear if the culture has CICM derived from both transgenic and nontransgenic, or if the claim is trying to further limit any CICM to one specifically derived from a transgenic bovine.

Claim 83 is unclear in the recitation of ‘comprises a multilayer portion’ because as reasoned for claim 82 above, the open language in claim 78 of a ‘stable culture comprising’ makes it unclear if the culture has CICM and a multilayer portion, or if the claim is trying to further limit nature or characteristic of the CICM in the culture to one specifically demonstrating a multilayer colony formation. It is noted that a cultured multilayer ICM colony is specifically defined on page 18 of the instant disclosure.

Claim 89 is unclear in the recitation of ‘a CICM cell line.’ Neither ‘stable culture’ nor ‘cell line’ is specifically defined in the specification, and in view of the art recognized definitions each of these terms are equivalent to each other. In view of the art recognized definitions, it is not clear how claim 89 further limits claim 78.

Art Unit: 1632

Double Patenting

Claim 90 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 79.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the instant case, it is unclear how claim 90 further limits the stable culture encompassed in claim 79. Since stable cultures and cell lines are recognized in the art to be essentially equivalent, claim 90 does not further limit claim 79 and thus, encompasses the same subject matter as claim 79.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Art Unit: 1632

Claims 79-85 and 90 are rejected under 35 U.S.C. 102(b) as being anticipated by Sims *et al.* (PNAS 90:6143-6147, 1993).

Claim 79 encompasses a stable culture of cultured inner cell mass (CICM) cells from bovine of one genetic complement. Claims 80-82 recite that the cells have been passaged at least 5-50 times and claim 90 recites that the stable culture is a cell line. Claim 83 encompasses a CICM derived from a transgenic bovine. Claims 85 and 86 are drawn to CICMs with specific physical properties. Claim 84 is directed to a CICM which is part of a multilayer cell mass.

First, in light of the teachings of the specification, the stable culture of CICM is defined as a cell similar to an ICM cell and is capable of developing embryos for prolonged culture periods, which is an inherent limitation of claim 79 for it to result in an animal. In view of this limitation, an CICM at passage 1 should be no different than at passage 50 or even at later passages. Therefore, even though they are a product by process claim the limitation of passage number does not qualitatively affect the CICM. Further, a cell derived from a transgenic bovine would still be a CICM cell, unless the transgene confers a particular phenotype to the CICM cell. Sims *et al.* teaches ICM cells in culture. The ICM cells are capable of giving rise to blastocyst and live born calves (Table 2 and 4). Sims *et al.* teach similar methods for the isolation of ICM as those disclosed in the instant specification, and in the description of the cells Sims *et al.* describe the morphology as 15-25 um (page 6144, top of second column), large nuclei to cytoplasm ratio and prominent nucleoli (page 6144, bottom of second column). Under nondifferentiating conditions the ICM cells aggregate and will form embryoid bodies (claim 83).

Art Unit: 1632

Sims *et al.* do not specifically state that the ICMs are alkaline protease positive and cytokeratin 18 negative, however in light of the similarity of isolation techniques and similarity in other morphologies, the ordinary artisan would expect that the ICM cells of Sims *et al.* would also be alkaline protease positive and cytokeratin 18 negative, and thus these properties would be inherent. It is noted that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433. See also *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985), *In re Ludtke*, 441 F.2d 660, 169 USPQ 563 (CCPA 1971), *Northam Warren Corp. v. D. F. Newfield Co.*, 7 F. Supp. 773, 22 USPQ 313 (E.D.N.Y. 1934) and MPEP 2112.01. In the instant case, the ICM cells taught by Sims *et al.* exhibit properties and meet the limitations recited in claims 79-86 and 90 and thus, anticipate the claims.

Claims 79-85 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Sims *et al.* (US Patent 6,107,543).

Art Unit: 1632

Claims 79-85 and 90 are summarized above. Patent '543 teaches essentially the same methods for isolation and ICM cells as in the PNAS reference. Briefly, Sims *et al.* teaches ICM cells in culture. The ICM cells are capable of giving rise to blastocyst and live born calves (Table 1 and 4). Sims *et al.* teach similar methods for the isolation of ICM as those disclosed in the instant specification. Sims *et al.* do not specifically describe the morphology of the cells in culture or that the ICMs are alkaline protease positive and cytokeratin 18 negative, however in light of the similarity of isolation techniques and similarity in other morphologies, the ordinary artisan would expect that the ICM cells of Sim *et al.* in '543 have the same characteristics as those discussed in the PNAS reference as outlined above, and thus these properties would be inherent. Thus, the ICM cells taught by Sims *et al.* anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1632

Claims 79-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims *et al.* (PNAS 90:6143-6147, 1993), Deboer *et al.* (US Patent 6,013,857) and Stewart *et al.* (Dev. Biol. 161,626-628, 1994).

Claims 79-85 and 90 are summarized above. Claims 84, 87-89 are directed to a CICM which is part of a multilayer cell mass and/or cultured in direct contact with fibroblast feeder cells.

Sims *et al.* is described above in detail. Briefly, Sims *et al.* teach methods of isolating ICM cells and specifically teach bovine ICM cells in culture. The ICM cells taught by Sims et al. were derived from a normal bovine, however they suggest that methodology could be extended and useful in the genetic modification of cattle (page 6146, bottom of second column). Deboer *et al.* teach at the time of filing methods for generating transgenic bovine were available. As noted above, it is not apparent that a CICM cell derived form a transgenic bovine would differ in its developmental properties from that derived from a bovine found in nature. The presence of a transgene does not alter the basic function of an CICM cell to promote development. However, if a distinguishable difference exists Deboer *et al.* teach a transgenic bovine from which ICM cells could be derived. The specific culturing methods of Sims *et al.* grow the bovine ICM cells in a disassociated suspension, not in the presence of fibroblast feeder cells. However, Sims *et al.* clearly indicate that further culturing systems which promote mitotic activity while inhibiting differentiation (page 6146, bottom of second column). In addition, Sims *et al.* teaches that most attempts to isolate and culture ICM cells are based on or adapted from the methods used to

Art Unit: 1632

culture mice cells (page 6143, middle of second column-referencing early work of Evans and coworkers). Stewart *et al.* teach the isolation of mouse stem cells and primordial germ cells, and their ability to contribute to the germ line (summarized in the abstract). In particular, Stewart *et al.* successfully maintain the isolated cells by culturing the isolated cells on fibroblast feeder cells (page 626, bottom of second column). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the methods taught in Stewart *et al.*, and used generally in the art to culture primordial cells and stem cells, for those taught in Sims *et al.* Sims *et al.* indicates the need for improved culturing methods and the indication that successful methods have been derived from those used in the mouse, and thus, one having ordinary skill in the art would have been motivated to substitute and optimize various successful methods used in the art for other ICM cells or ES cells derived from other species than mouse. There would have been a reasonable expectation of success given the successful results of Stewart *et al.* in culturing various sources of stem/primordial cells to extend and optimize if necessary culture conditions which maintain bovine ICM cells capable of contributing to the germ line.

Thus, absent evidence to the contrary, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Art Unit: 1632

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732.

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608.

An inquiry of a general nature or relating to the status of the application should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Deborah Crouch

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